USSN: 09/732,348

Atty. Dkt. No.: 8325-2012 Client Dkt. No.: G12-US1

REMARKS

STATUS OF THE CLAIMS

Claims 24, 27-33, 35-39, 41-43, 48-50 and 71 were pending as shown in the response filed April 26, 2006. By amendment herein, claim 24 has been amended to recite a target sequence in a plant gene. Support for the amendment can be found throughout the specification as filed, for example, on pages 20-22. Thus, claims 24, 27-33, 35-39, 41-43, 48-50 and 71 are pending and claims 24, 27-29, 32, 33, 35-39, 41, 42, 48-50 and 71 are under consideration.

Applicants note that, in a Restriction Requirement dated December 28, 2004, claim 24 was identified as linking Groups A-E and that Groups B-E included claims 30 and 31.

Applicants subsequently elected Group A, with traverse. Accordingly, upon allowance of claim 24, that Restriction Requirement shall be withdrawn and claims 30 and 31, which contain all the limitations of claim 24, shall be rejoined.

Furthermore, a Restriction Requirement dated July 16, 2002, contained the following two groups:

III: [then-pending] claims 15 and 22, drawn to plant host cells and transgenic plants comprising a polynucleotide encoding an engineered zinc finger polypeptide fused to a transcriptional activator domain

and

IV: [then-pending] claims 16 and 23, drawn to plant host cells and transgenic plants comprising a polynucleotide encoding an engineered zinc finger polypeptide fused to a transcriptional repressor domain.

That Restriction Requirement also stated that then-pending claims 7 and 8 (directed to plant host cells and transgenic plants, respectively, comprising a polynucleotide encoding an engineered zinc finger polypeptide and a target DNA sequence to which the zinc finger polypeptide binds) linked groups III and IV.

Inasmuch as presently-pending claim 43 was said to be directed to the invention of non-elected Group IV (see Office Action dated December 28, 2004 at page 2), and presently-pending claim 24 corresponds to previously-pending claims 7 and 8, claim 24 links groups III and IV.

USSN: 09/732,348

Atty. Dkt. No.: 8325-2012 Client Dkt. No.: G12-US1

Accordingly, upon allowance of claim 24, that Restriction Requirement shall be withdrawn and claim 43 shall be rejoined.

ALLOWABLE CLAIMS

Applicants note that claims 27, 28, 29 and 71 were objected to as being dependent upon a rejected base claim but would be allowable if rewritten in independent form.

35 U.S.C. § 102

Claims 24, 32-33, 35-37, 39, 41-42 and 49-50 were again rejected, and claim 38 was newly rejected, under 35 U.S.C. § 102(e) as allegedly anticipated by U.S. Patent No. 6,534,261 (hereinafter "Cox"). See, e.g., pages 2-3 of the Office Action, citing the VEGF1 and VEGF3a zinc finger proteins disclosed at column 41, line 5 through column 42, line 9 of Cox. Again, it was maintained that Cox's VEGF ZFP <u>may</u> bind to and regulate a gene in a plant cell. (Office Action, page 3). Thus, Cox was alleged to "teach all of the required technical features set forth in the rejected claims." *Id*.

In fact, the Office has not met its burden of showing that Cox's VEGF protein binds to a target sequence in a plant gene, as claimed. Therefore, Cox does not teach all the technical features of the pending claims.

As previously noted, Cox's VEGF3a and VEGF1 ZFPs bind to particular target sequences in a human VEGF gene, specifically depicted in SEQ ID NO:13 of Cox (see, col. 40, line 50). As shown in the attached BLAST searches (attached hereto as Appendix A), the target sequences of Cox's VEGF ZFPs (NGGGGAGGATN and NGCGGAGGCTN, where "N" is any nucleotide) are **not** present in the *Arabidopsis* genome. Consequently, Cox's VEGF3a and VEGF1 proteins do not necessarily and inevitably bind to a target sequence in a plant gene. Therefore, Cox fails to anticipate any of the pending claims and Applicants respectfully request withdrawal of the rejection.

The Office also asserts that "plants need not have native endogenous VEGF genes in order for Cox et al. to anticipate the rejected claims, as the transformation of plants with heterologous genes *including human genes* was established in the art at the time of Cox et al.'s

USSN: 09/732,348 Atty. Dkt. No.: 8325-2012

Client Dkt. No.: G12-US1

invention . . ." (Office Action at page3, emphasis added). Applicants are not aware that the introduction of human genes into plants was routine in the art as of January 1999, and the Office has not provided any evidence to support this assertion. Thus, in order for the rejection to be maintained, the Office must provide evidence that transformation of plants with human genes was established in the art in January 1999. Alternatively, an affidavit pursuant to 37 C.F.R. § 1.104(d)(2) must be provided. See also MPEP 2144.03.

Finally, inasmuch as applicants have presented evidence that the target sequences of the engineered zinc finger proteins disclosed by Cox are not necessarily and inevitably present in a plant cell, the only remaining possible basis for the rejection is the hypothetical introduction of some gene, containing the target sequences of the VEGF3a or VEGF1 proteins, into a plant cell. However, the Office has not pointed to any motivation for one of skill in the art to introduce such a hypothetical gene into a plant cell, least of all a human VEGF gene containing the sequences bound by Cox's proteins.

For all of the aforementioned reasons, the rejection is improper and should be withdrawn.

35 U.S.C. § 103

Claim 48 was rejected under 35 U.S.C. § 103(a) as allegedly obvious over Cox in view of Kim and Puchta. (Office Action, pages 4-5). In support of the rejection, the Examiner stated, in part, that "plants do not need to have endogenous VEGF genes in order for the combined references to render obvious the claimed subject matter as the transformation of plants with heterologous genes including human genes was established in the art at the time of Cox's invention, and the teachings of Cox are not limited to the regulation of native endogenous genes in plant cells." (Office Action, page 4).

Contrary to the Examiner's assertions, claim 48 does not encompass plant cells in which a fusion of a ZFP and a catalytic domain of a restriction enzyme binds to a target sequence in a human.gene that has been introduced into a plant cell. Rather, pending claim 48 requires that the target sequence is in a plant.gene. As noted above, the target sequences of Cox's human VEGF gene-binding ZFP are not present in the Arabidopsis.genome. Thus, there is no motivation to

USSN: 09/732,348 Atty. Dkt. No.: 8325-2012

Client Dkt. No.: G12-US1

combine Cox's VEGF ZFP with Kim and/or Puchta and no combination of these references that would result in the subject matter of claim 48. Accordingly, withdrawal of the rejection of this claim is in order.

In addition, and as stated above, the Office's assertion that "transformation of plants with heterologous genes including human genes was established in the art at the time of Cox's invention" has not been supported by evidence or affidavit.

Finally, the Office Action states that one of skill in the art would have been motivated to combine Cox with Kim and Puchta to increase the frequency of homologous recombination at a specific locus. However, the Office has failed to show that the art provides any motivation for one of skill in the art to want to increase the frequency of homologous recombination in plants; thus failing to make a *prima facie* case of obviousness. For this reason, as well, the rejection should be withdrawn.

USSN: 09/732,348 Atty. Dkt. No.: 8325-2012

Client Dkt. No.: G12-US1

CONCLUSION

In view of the foregoing amendments, Applicants submit that the claims are now in condition for allowance and request early notification to that effect, as well as rejoinder of claims 30, 31 and 43.

Respectfully submitted,

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